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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,304	04/20/2007	Naoki Kimura	14875-166US1 CI-A0323P-US	4817

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EXAMINER	
GUSSOW, ANNE	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
03/24/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/582,304	KIMURA ET AL.	
	Examiner	Art Unit	
	Anne M. Gussow	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,17-24 and 29-46* is/are pending in the application.

4a) Of the above claim(s) *17-21,29-31 and 35-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,22-24 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/31/09, 1/13/10, 2/22/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 3, 4, 21, and 23 have been amended.

Claims 11-16 and 25-28 have been cancelled.

Claims 17-21, 29-31, and 35-46 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on December 16, 2008.

2. Claims 1-10, 22-24, and 32-34 are under examination.

3. The following office action contains NEW GROUNDS of Rejection.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on October 13, 2009, January 13, 2010, and February 22, 2010 were filed after the mailing date of the non-final rejection on September 15, 2009. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner and an initialed copy of the IDS is included with the mailing of this office action.

5. The proprietary IDS filed on January 11, 2010 has been fully considered by the examiner. Due to the proprietary nature of the IDS, an initialed copy will not be included in the file wrapper.

Rejections Withdrawn

6. The rejection of claims 1-10, 22-24, and 32-34 under 35 U.S.C. 103(a) as being obvious over Ozaki, et al. in view of Kortt, et al. is withdrawn in view of the new grounds of rejection. The examiner does not acquiesce applicant's position. Relevant portions of applicant's arguments will be discussed as part of the new rejection.

NEW GROUNDS of Rejection

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-10, 22-24, and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ozaki, et al. (Blood, 2003. Vol. 102, page 933a, as cited on the IDS filed May 31, 2007) in view of Beresford, et al. (International Journal of Cancer, 1999. Vol. 81, pages 911-917), as evidenced by the specification.

The claims recite an antibody comprising two heavy chain variable regions and two light chain variable regions, wherein the antibody is a single chain polypeptide having a binding activity against human leukocyte antigen (HLA), wherein the two heavy chain variable regions and two light chain variable regions are arranged in the order of heavy chain variable region, light chain variable region, heavy chain variable region, and light chain variable region, starting from the N terminus of the single chain polypeptide, further comprising linkers between the variable regions, wherein each of the linkers comprise 15 amino acids, wherein HLA is HLA class I, wherein HLA class I is

HLA-A, wherein the antibody is sc(Fv)2. An sc(Fv)2 comprising heavy chain variable regions that comprise CDR 1, 2, and 3 consisting of the amino acid sequences of SEQ ID NOs: 3, 4, and 5. An sc(Fv)2 comprising light chain variable regions that comprise CDR 1, 2, and 3 consisting of the amino acid sequences of SEQ ID NOs: 6, 7, and 8. An sc(Fv)2 comprising heavy chain variable regions that comprise CDR1, 2, and 3 consisting of the amino acid sequences of SEQ ID NOs: 3, 4, and 5, and light chain variable regions that comprise CDR 1, 2, and 3 consisting of the amino acid sequences of SEQ ID NOs: 6, 7, and 8. A pharmaceutical composition comprising the antibody of claim 1 as an active ingredient, wherein the antibody has cell death inducing activity against B cells or T cells, wherein the B cells or T cells are activated B cells or activated T cells. A pharmaceutical composition comprising the sc(Fv)2 of claim 8 as an active ingredient. A pharmaceutical composition comprising the sc(Fv)2 of claim 9 as an active ingredient. A pharmaceutical composition comprising the sc(Fv)2 of claim 10 as an active ingredient.

Ozaki, et al. teach a recombinant scfv diabody which binds to HLA and has a cell death inducing function, a cell growth inhibitory function, and an anti myeloma (blood tumor) function. Ozaki, et al. teach a 2D7 antibody clone which binds to HLA and has a cell death inducing function, a cell growth inhibitory function, and an anti-myeloma (blood tumor) function. The specification discloses the 2D7 antibody clone was used to produce the sc(Fv)2 as instantly claimed (see page 2 lines 26-36). Thus, the sequence of the Ozaki, et al. antibody and the instantly claimed SEQ ID Nos. 3-8 would

necessarily be identical. Ozaki, et al. do not teach an sc(Fv)2 antibody. This deficiency is made up for in the teachings of Beresford, et al.

Beresford, et al. teach production of sc(Fv)2 antibodies that have higher tumor uptake and retention than scFv (table 1 and page 915 bottom of 2nd column to page 916).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antibody of Ozaki, et al. to produce an sc(Fv)2 which maintained the cell death inducing, cell growth inhibiting and anti myeloma functions in view of Beresford, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antibody of Ozaki, et al. to produce an sc(Fv)2 which maintained the cell death inducing, cell growth inhibiting and anti myeloma functions in view of Beresford, et al. because Beresford, et al. teach that sc(Fv)2 molecules had higher tumor uptake and longer retention time than scFv molecules.

Regarding the sequences in claims 8-10, applicants arguments are directed to the operability of the prior art. Ozaki, et al. teach an antibody clone 2D7 that binds to HLA the specification discloses that the 2D7 antibody clone that binds to HLA was used to produce the sc(Fv)2 as instantly claimed (see page 2 lines 26-36). When the reference relied on expressly anticipates all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. In re Sasse,

629 F.2d 675, 207 USPQ 107 (CCPA 1980). (see MPEP 2121). Since the authors of the Ozaki reference are different from the instant inventive entity, it is presumed that the 2D7 antibody was available to the public. Further, it is routine in the art to determine the sequence of a protein, therefore, one of ordinary skill in the art would have been able to determine the sequence of the Ozaki, et al. antibody to enable manipulation of the antibody into various forms including sc(Fv)2.

Regarding the pharmaceutical composition of claims 22-24 and 32-34, the pharmaceutical composition is an intended use of the claimed antibody and as such receives no patentable weight.

Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antibody of Ozaki, et al. to produce an sc(Fv)2 which maintained the cell death inducing, cell growth inhibiting and anti myeloma functions in view of Beresford, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
March 17, 2010

/Anne M. Gussow/
Examiner, Art Unit 1643